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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
DECLOUX, AMY M

ART UNIT	PAPER NUMBER
1644	19

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/840,243	MASTERNAK ET AL.	
	Examiner	Art Unit	
	Amy M. DeCloux	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-76* is/are pending in the application.

4a) Of the above claim(s) *7-61 and 67-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6 and 62-66* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9, 15.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group 1, claims 1-6 and 62-66, in Paper No. 18, filed 12-4-02, is acknowledged.

Claims 7-61 and 67-76 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 18, filed 12-4-02.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Specifically non-initialed alterations in Inventor Masternak's residence, post office address and citizenship are noted, as well as non-initialed changes in Inventor Reith's residence and post office address.

Claim Objections

A. Claim 2 is objected to because of the following informalities: the phrase "wherein the cells are BLS cell line, Na cell line or Ba cell line", recited in Claim 2 appears to be missing the word "from" after the word "are" because cells are not a cell line. Appropriate correction is required.

B. Claim 5 is objected to because of the following informalities: the phrase "in another species than human" is awkward. Perhaps substituting the phrase "in a species other than human" could be considered.

Specification

A. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Specifically, hyperlinks are disclosed on page 55, lines 23-24., on page 56.

B. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Specifically the nucleic acid sequences disclosed on page 67 of the specification lack SEQ ID NO: tags. Applicants are required to resubmit a substitute disk and paper copy of the sequences according to the attached "Notice to Comply with the Sequence Rules." Applicant is reminded of the sequence rules which require a submission for all sequences of more than 9 nucleotides or 3 amino acids (see 37 C.F.R. 1.821-1.825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules.

C. The abstract of the disclosure is objected to because the abstract contains the word "novel". Patents are presumed to be novel. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Correction is required. See MPEP § 608.01(b).

D. The Title of the application is objected to because of the inclusion of the word "new". Patents are presumed to be novel. The word "new" in the title must be deleted.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Europe on 10/24/1998. It is noted, however, that applicant has not filed a certified copy of the European application as required by 35 U.S.C. 119(b).

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. Specifically, reference is made to the list of references disclosed on pages 74-86.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 1-3 and 5-6 and 62-66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant disclosure of the human amino acid sequence of SEQ ID NO:2 does not provide adequate written description for the genus of peptides or proteins capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and comprising all or part of the amino-acid sequence shown in Figure 2, as recited in claims 1-3, or for the genus of proteins or peptides which is the homologous, non-human protein of a protein or peptide capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and comprising all or part of the amino-acid sequence shown in Figure 2, as recited in claims 5-6, or for the genus of proteins or peptides that has at least 80% or 90% identity, similarity or homology with the amino acid sequence shown in Figure 2, as recited in claims 62-63 and 65-66.

The instant specification discloses in Figure 2, a protein consisting of SEQ ID NO:2 that is capable of restoring the MHC-II expression in cells from MHC II deficiency patients in complementation group B.

It is noted by the examiner that though the claimed invention is directed to a protein or peptide, and not cDNA, the principle of the following still holds for the genus of said protein or peptide: a description of a genus of cDNAs may be achieved by means of a recitation of a

representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly&Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Accordingly, the disclosure of one species of a genus (the FRXANK protein of SEQ ID NO:2) is not equivalent to a representative number of species. Also, the structural features common to the genus of peptides or proteins capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B, which features constitute a substantial portion of said genus, are not disclosed. Therefore, one of skill would not be able to discern which proteins or peptides, other than a protein or peptide having the amino acid sequence of SEQ ID NO:2, would be capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B, and thus would be encompassed by the instant claims 1-3 and 5-6, nor which proteins or peptides comprise a functional part of SEQ ID NO:2 and thus would be encompassed by the instant claim 64, without further description form the specification.

Claims 5-6 recite a protein or peptide, which is the homologous protein of a protein or a peptide of Claim 1 in another species than human, such as pig. However, since the Applicants have not disclosed RFXANK polypeptide from any other species besides human the invention encompassing all species of mammal is not adequately described. Further, by reciting percent identity, similarity, and homology language in claims 62-63 and 65-66, an innumerable number of additions, deletions, substitutions and combinations thereof, is encompassed by the instant claims, and one of skill would not be able to discern which peptides and proteins are encompassed by the claimed genus, without further description form the specification.

Therefore, the disclosure of the human amino acid sequence of SEQ ID NO:2 is not sufficient to provide adequate written description for the breadth of the claimed genus of peptides and proteins.

B. Claims 1-3 and 5-6 and 62-66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein or peptide consisting of SEQ ID NO:2, which is capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B, does not reasonably provide enablement for any peptide or protein capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B, wherein said peptide or protein comprises any part of the amino acid sequence shown in Figure 2, other than SEQ ID NO:2, or for any protein or peptide which is the homologous, non-human protein of any protein or peptide capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and comprising all or part of the amino-acid sequence shown in Figure 2, other than SEQ ID NO:2, or for any protein or peptide that has at least 80% or 90% identity, similarity or homology with the amino acid sequence shown in Figure 2, other than SEQ ID NO:2.

The instant claims are drawn to a peptide or protein capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and comprising all or part of the amino-acid sequence shown in Figure 2, as recited in claims 1-3, a protein or peptide which is the homologous, non-human protein of a protein or peptide capable

of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and comprising all or part of the amino-acid sequence shown in Figure 2, as recited in claims 5-6, and a protein or peptide that has at least 80% or 90% identity, similarity or homology with the amino acid sequence shown in Figure 2, as recited in claims 62-66.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The instant specification discloses on pages 59 and 60 and Figure 4, that the cell lines BLS1, Na and Ba are each from a patient in complementation Group B, and that transfection into these cell lines of plasmid pEBO-RFXANK which comprises the coding region for the amino acid sequence of SEQ ID NO:2, restores MHC Class II expression.

The instant specification discloses on pages 5-11 that MHC Class II genes are co-regulated at the level of transcription by a 150 bp regulatory module conserved in their promoter proximal regions, and that this module contains four sequences, the W, X, X2 and Y boxes, and that three distinct multi-protein transcription factors RFX, X2BP and NF-Y bind cooperatively to the X, X2 and Y boxes, and that said factors, together with the factor CIITA, are essential for MHC Class II transcription. The instant specification also discloses on page 5 that RFXANK encoded by SEQ ID NO:2 is a novel component of the RFX complex, that RFXANK has a dramatic effect on the binding of the RFX complex to the X box motif, and that the RFX components of RFXANK, RFX5 and RFXAP are required for RFX binding. However, as disclosed on pages 5-6, it is not known with exactly which molecules RFXANK interacts. Without this knowledge it would require undue experimentation for one of skill to predict which part of SEQ ID NO:2 would be capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B without further guidance from the specification. And accordingly, it would require undue experimentation for one of skill to predict which combination of amino acid additions, deletions, and substitutions of SEQ ID NO:2, encompassed by the recited percent identity, similarity, and homology language, would be capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B without further guidance from the specification, because the specification does not disclose what changes in the amino acid sequence of SEQ ID NO:2 affect its ability to restore MHC-II expression in cells from MHC-II deficiency patients in complementation group B. The problem of predicting functional aspects of the protein product in terms of what changes can be tolerated is complex and well outside the realm of routine experimentation. This complexity is due in part to the fact that the relationship between the amino acid sequence of a peptide (and its corresponding encoding nucleic acid sequence) and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo et al., (V), newly cited, in The Protein Folding Problem and Tertiary Structure Prediction,1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495).

Besides the protein consisting of the amino acid sequence of SEQ ID NO:2, the specification fails to provide guidance as to how to derive a "homologous protein" of a protein or peptide capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and comprising all or part of the amino-acid sequence shown in

Figure 2 using the instant disclosure. The instant specification discloses on page 15 that the amino acid sequence of RFX-ANK of species other than human can be obtained by standard methods like cross hybridization at low stringency. However it is noted that Skolnick et al (Trends in Biotech. 18(1):34-39, 2000) who teach that assigning functional activities for any protein based upon sequence homology is inaccurate, in part because of the multi-functional nature of polypeptide (see entire article, including the Abstract and page 34). Therefore, screening large numbers of polynucleotides encoding a "homologous protein" capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and comprising all or part of the amino-acid sequence shown in Figure 2, is unpredictable and would require undue experimentation without further guidance from the instant specification.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue experimentation to make and use the peptides or proteins of the claimed invention.

C. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the cell lines BLS1, Na and Ba are required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of *35 U.S.C. 112*, first paragraph, may be satisfied by a deposit of said cell lines. *See 37 C.F.R. 1.802.*

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. *See 37 C.F.R. 1.808.*

In addition, the identifying information set forth in *37 C.F.R. 1.809 (d)* should be added to the specification. *See 37 C.F.R. 1.803-1.809* for additional explanation of these requirements, Amendment of the specification to disclose the date of deposit and the complete name and address of the depository is required (ATCC, 10801 University Boulevard, Manassas, VA 20110-2209).

If the deposit was made after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the plasmid described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from Applicant to the depository coupled with corroboration that the deposit is identical to the biological material

described in the specification and in the Applicant's possession at the time the application was filed.

Applicant's attention is directed to *In re Lundak*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985), and 37 C.F.R. 1.801-1.809 for further information concerning deposit practice.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 64-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 2 recites the limitation "Ba cell line" in line 2. There is insufficient antecedent basis for this limitation in the claim. It is noted that there are numerous examples of the cell line Ab disclosed in the specification, such as on pages 11 and 60.

B. Claims 64-66 are indefinite in their recitation of the phrase "functional part" because the specification discloses on page 13 that the phrase "functional part" in exemplary form. Incorporating a specific function into the claims would overcome this rejection.

C. Claims 65 and 66 are indefinite in their recitation of the phrases "has at least 80% homology" and "has at least 90% homology", respectively, because the criteria for determining percent homology are not disclosed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 5-6 and 62-66 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al (US Patent 5,989,863, issued 11-23-1999, filed 10-14-1998).

'863 teaches a human ankyrin family protein (designated ANFP) that consists of an amino acid sequence (SEQ ID NO:1) identical to the amino acid sequence of the instantly disclosed SEQ ID NO:2, (see entire patent, especially the Abstract, and Figures 1 and 2, and column 3). Though the referenced patent does not disclose the limitations that said protein is capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and that it comprises all or part of the amino acid sequence of instant

SEQ ID NO:2, the referenced protein would have said limitations because the amino acid sequence of the referenced protein is identical to that of the claimed protein. Claims 5 and 6 are included because '863 discloses in column 4, lines 35-43, the amino acid sequences of substantially pure ANFP from any species including porcine (pig). Therefore, the referenced teaching anticipates the claimed invention.

Conclusion

Claim 4 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703 872-9306 for regular communications and 703 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Amy DeCloux, Ph.D.,
Patent Examiner, Group 1640,
March 23, 2003

Amy DeCloux
3-23-03